

The following listing of claims are the claims presented in this application.

LISTING OF THE CLAIMS:

Claims 1-45 (Canceled)

Claim 46 (New): A method of generating tissue in a patient comprising:

culturing human cells which are differentiated to a point where they are programmed to develop into a specific type of cell in a liquid culture medium which is replaced at a rate of at least 25% daily replacement continuously for more than one day and for a time sufficient to obtain lineage committed with enhanced biological function, which is relative to the biological function of the human cells that are cultured in static culture; and

transferring said cultured cells into said patient to generate said tissue.

Claim 47 (New): The method of claim 46, wherein the culture medium is continuously perfused at a ramped rate proportional to the lactate concentration and/or cell density to replace the culture medium without substantial dilution of the cell density.

Claim 48 (New): The method of claim 46, wherein replacement of said medium comprises perfusing fresh medium through at least part of the mass of said human cells.

Claim 49 (New): The method of claim 46, wherein said medium comprises animal or human sera or plasma.

Claim 50 (New): The method of claim 46, comprising maintaining glucose concentration in said medium in the range of from 5 to 20 mM, lactate concentration in said medium below about 35 mM, glutamine concentration in said medium in the range of from 1 to 3 mM, and ammonia concentration in said medium below 2.4 mM.

Claim 51 (New): The method of claim 46, further comprising removing nonadherent cells continuously, periodically, or intermittently, without disturbing adherent cells.

Claim 52 (New): The method of claim 46, wherein the tissue formed is any of human bone marrow, human blood, human immune system, human bone, human cartilage, human vascular tissue, human muscle, human pancreatic cells, human nerves or human epithelial tissue.

Claim 53 (New): The method of Claim 46, wherein said human cells are selected from the group consisting of hepatocytes, neural cells, epithelial cells, keratinocytes, endothelial cells and mesenchymal cells.

Claim 54 (New): The method of Claim 53, wherein said human lineage committed tissue cells are mesenchymal cells.

Claim 55 (New): The method of Claim 54, wherein said mesenchymal cells are selected from the group consisting of chondrocytes, osteoblasts, myoblasts, fibroblasts, tenoblasts, bone marrow stromal cells, tenocytes, adipocytes, osteocytes, and myocytes.

Claim 56 (New): The method of claim 46, wherein replacement of said medium comprises perfusing fresh medium through at least part of the mass of said human stem cells.

Claim 57 (New): The method of Claim 46, wherein the liquid medium is replaced at a rate equal to 50 to 100% daily replacement for a cell density of from 1×10^4 to 1×10^7 cells per ml of culture.

Claim 58 (New): The method of claim 57, wherein said medium comprises animal human sera or plasma.

Claim 59 (New): The method of claim 57, comprising maintaining glucose concentration in said medium in the range of from 5 to 20 mM, lactate concentration in said medium below about 35 mM, glutamine concentration in said medium in the range of from 1 to 3 mM, and ammonia concentration in said medium below 2.4 mM.

Claim 60 (New): The method of claim 57, further comprising removing nonadherent cells continuously, periodically, or intermittently, without disturbing adherent cells.

Claim 61 (New): The method of Claim 57, wherein said human lineage committed tissue cells are selected from the group consisting of hepatocytes, neural cells, epithelial cells, keratinocytes, endothelial cells and mesenchymal cells.

Claim 62 (New): The method of Claim 61, wherein said human lineage committed tissue cells are mesenchymal cells.

Claim 63 (New): The method of Claim 62, wherein said mesenchymal cells are selected from the group consisting of chondrocytes, osteoblasts, myoblasts, fibroblasts, tenoblasts, bone marrow stromal cells, tenocytes, adipocytes, osteocytes, and myocytes.

Claim 64 (New): The method of Claim 46, wherein the human cells are cultured for at least 2 days.

Claim 65 (New): The method of Claim 46, wherein the culture medium contains at least 1 growth factor which stimulates the proliferation of the cells.

Claim 66 (New): A method of providing a therapeutic benefit to a patient comprising:
culturing human cells which are differentiated to a point where they are programmed to develop into a specific type of cell in a liquid culture medium which is replaced at a rate of at least 25% daily replacement continuously for more than one day and for a time sufficient to obtain lineage committed with enhanced biological function, which is relative to the biological function of the human cells that are cultured in static culture; and
transferring said cultured cells into said patient.

Claim 67 (New): The method of claim 66, wherein the culture medium is continuously perfused at a ramped rate proportional to the lactate concentration and/or cell density to replace the culture medium without substantial dilution of the cell density.

Claim 68 (New): The method of claim 66, wherein replacement of said medium comprises perfusing fresh medium through at least part of the mass of said human cells.

Claim 69 (New): The method of claim 66, wherein said medium comprises animal or human sera or plasma.

Claim 70 (New): The method of claim 66, comprising maintaining glucose concentration in said medium in the range of from 5 to 20 mM, lactate concentration in said medium below about 35 mM, glutamine concentration in said medium in the range of from 1 to 3 mM, and ammonia concentration in said medium below 2.4 mM.

Claim 71 (New): The method of claim 66, further comprising removing nonadherent cells continuously, periodically, or intermittently, without disturbing adherent cells.

Claim 72 (New): The method of claim 66, wherein the tissue formed is any of human bone marrow, human blood, human immune system, human bone, human cartilage, human vascular tissue, human muscle, human pancreatic cells, human nerves or human epithelial tissue.

Claim 73 (New): The method of Claim 66, wherein said human cells are selected from the group consisting of hepatocytes, neural cells, epithelial cells, keratinocytes, endothelial cells and mesenchymal cells.

Claim 74 (New): The method of Claim 73, wherein said human lineage committed tissue cells are mesenchymal cells.

Claim 75 (New): The method of Claim 74, wherein said mesenchymal cells are selected from the group consisting of chondrocytes, osteoblasts, myoblasts, fibroblasts, tenoblasts, bone marrow stromal cells, tenocytes, adipocytes, osteocytes, and myocytes.

Claim 76 (New): The method of claim 66, wherein replacement of said medium comprises perfusing fresh medium through at least part of the mass of said human stem cells.

Claim 77 (New): The method of Claim 66, wherein the liquid medium is replaced at a rate equal to 50 to 100% daily replacement for a cell density of from 1×10^4 to 1×10^7 cells per ml of culture.

Claim 78 (New): The method of claim 77, wherein said medium comprises animal human sera or plasma.

Claim 79 (New): The method of claim 77, comprising maintaining glucose concentration in said medium in the range of from 5 to 20 mM, lactate concentration in said medium below about 35 mM, glutamine concentration in said medium in the range of from 1 to 3 mM, and ammonia concentration in said medium below 2.4 mM.

Claim 80 (New): The method of claim 77, further comprising removing nonadherent cells continuously, periodically, or intermittently, without disturbing adherent cells.

Claim 81 (New): The method of Claim 77, wherein said human lineage committed tissue cells are selected from the group consisting of hepatocytes, neural cells, epithelial cells, keratinocytes, endothelial cells and mesenchymal cells.

Claim 82 (New): The method of Claim 81, wherein said human lineage committed tissue cells are mesenchymal cells.

Claim 83 (New): The method of Claim 82, wherein said mesenchymal cells are selected from the group consisting of chondrocytes, osteoblasts, myoblasts, fibroblasts, tenoblasts, bone marrow stromal cells, tenocytes, adipocytes, osteocytes, and myocytes.

Claim 84 (New): The method of Claim 76, wherein the human cells are cultured for at least 2 days.

Claim 85 (New): The method of Claim 76, wherein the culture medium contains at least 1 growth factor which stimulates the proliferation of the cells.

Claim 86 (New): The method of Claim 66, wherein the therapeutic benefit provided to the patient is generation of a tissue.